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PRINCIPAL INVESTIGATOR: Beth A. Jones, Ph.D.

CONTRACTING ORGANIZATION: Yale University  
New Haven, Connecticut 06520-8047

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<b>13. ABSTRACT (Maximum 200 Words)</b> <p>This is a population based follow-up study of 145 African American (AA) and 177 white (W) women who were diagnosed with breast cancer between January, 1987 and May, 1989. As of January, 1999, 135 (41.9%) of the women had died. Survival among AA women (56.9%) was significantly lower than survival in W women (68.9%) [age-adjusted Risk Ratio {RR} 1.73 (95% Confidence Interval {CI} 1.21 - 2.48)]. The significant survival disadvantage persisted even with additional adjustment for TNM stage at diagnosis and one measure of socioeconomic status (education) (RR 1.49, 95% CI 1.02 - 2.19). African American women were twice as likely to be diagnosed with tumors that were TNM stage II or higher. Evaluating archived tissue specimens, we demonstrated some important race differences: AA women were significantly more likely than W women to have tumors that were higher histologic grade, higher nuclear grade, estrogen receptor negative, and p53 positive, all of which are associated with poor prognosis. Although AA women were more likely than W women to be progesterone receptor negative (61% vs. 50%), and to express c-met (62% vs. 56%), these differences were not statistically significant. AA women were not significantly to be positive for HER-2(neu). Summary: AA women were more than were W women to die from their breast cancer in the approximately 10 year follow-up period. Tumors in African American women were more likely to be to have characteristics associated with poor prognosis than were white women. The race difference in TNM stage at diagnosis was the strongest explanatory factor for the observed race difference in survival. Race difference in socioeconomic status was not an important explanatory variable. After adjustment for TNM stage at diagnosis, the factors that predict survival may be race specific.</p>				
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## INTRODUCTION

### *Background*

Despite recent improvements in breast cancer mortality rates in the general population, the improvement in these rates is less impressive for African American women than for White women. In part, this is due to the persistent racial difference in five-year relative survival rates. The five-year relative survival rate for African American women for the period, 1989-1996: Whites, 86% vs. blacks, 71%. (Greenlee, 2001). While it is known that the later stage at diagnosis in African American breast cancer cases compared with White breast cancer cases plays a major role in the survival difference, race disparities within each stage at diagnosis exist. This is a follow-up study of a cohort of African American and white women who were diagnosed with breast cancer in the late 1980s. Specifically, we are investigating race differences in a wide ranging group of variables and their explanatory role(s) in the observed race /ethnic difference in breast cancer survival. We are investigating the prognostic importance of sociodemographic, medical care, and psychosocial factors as well as tumor characteristics and selected genetic alterations. In this investigation, we have combined retrospective epidemiologic data (previously collected interview data) and data on established prognostic indicators (e.g., tumor stage) with new molecular data derived from tissue blocks to predict survival from breast cancer. Findings from this investigation may lead to a better understanding of the means to achieve a reduction in mortality from breast cancer, with special application to African American women.

### PROGRESS TO DATE:

Using a previously established population-based cohort of 322 breast cancer cases (145 black women, 177 white women), we retrieved archived tissue tumor and collected new data on treatment, recurrence, second primaries, and vital status. Of the original Technical Objectives, the following have been completed.

1. Examined African American / White differences in survival approximately 10 years after diagnosis.
2. Examined African American / White differences in specific genetic alterations, using archived tissue specimens from the original biopsy and/or mastectomy. Specifically, race differences in the frequency of p53 mutations and frequency of overexpression of Her-2 (neu) were determined. Tumors that are determined to be positive for p53 mutations were further examined to determine the type and location of those mutations. We also conducted assays to determine the prognostic significance of c-met and phospho-neu (neither were part of original protocol).
3. Examined African American / White differences in a number of tumor characteristics that are more established prognostic indicators: histopathologic tumor grade, nuclear grade, DNA ploidy, S phase fraction, estrogen receptor status, and progesterone receptor status (also using archived tumor tissue). Other prognostic variables that were available from the original pathology reports and expert review included: TNM tumor stage, tumor size, lymph node status, presence of distant metastasis, and of lesser prognostic importance, lymphatic invasion,

necrosis, and skin involvement.

4. Determined the relationship of all variables mentioned above (i.e., genetic alterations and more conventional prognostic variables) and treatment variables, as well as those that were collected by interview at the time diagnosis (e.g., socioeconomic status, comorbidity and obesity, medical care and insurance factors, and psychosocial variables) to survival in the total population, and by race group. These relationships are being examined in multivariate analyses.

The last two technical objectives represent work that involves complicated statistical analysis and is still ongoing:

5. Identify the constellation of prognostic variables that explain the African American / White difference in survival. Since it is known that tumor stage and its components play a large role in the observed race difference in survival, the primary objective is to identify factors that explain the portion of the African American / White survival differential not accounted for by race differences in stage at diagnosis.

6. Although the primary outcome of this investigation is survival, the proposed analysis of tumor tissue will also provide an opportunity to evaluate the relationship of p53 mutations and overexpression of HER2 (neu) {erbB-2} to tumor stage at diagnosis and its components (tumor size and lymph node status). In addition, the relationship between molecular alterations and risk factors such as reproductive history, family history of breast cancer, use of oral contraceptives and other estrogens, alcohol consumption, and smoking will be examined.

#### **PROGRESS TO DATE WITH RESPECT TO ORIGINAL STATEMENT OF WORK**

Task 1: Month 1-1.5: Hire project coordinator/ **COMPLETED**

Task 2: Months 1-6: Submit protocol to 22 hospitals to gain approval from the Institutional Review Boards. This requires a significant amount of paperwork as well as personal appearances by the P.I. and the RCA director. **COMPLETED**

Task 3: Months 1-12: Develop and learn a data tracking system. This will be preceded by the purchasing of a new computer and appropriate software. **COMPLETED**

Task 4: Months 1-3: Review all existing files on patients to establish a comprehensive list of hospitals in which tumor specimens might be located. This is not a task that can be computerized, because the existing data is part of original documentation that was abstracted from patients' medical charts. **COMPLETED**

Task 5: Months 7-9: Collect tumor specimens from 22 hospitals. **COMPLETED**

Task 6: Months 7-9: Link study cases to Connecticut Tumor Registry files. **COMPLETED IN 1997; DATA INCLUDED IN PRELIMINARY RESULTS PRESENTED AT ERA OF HOPE MEETINGS**

**UPDATE:**

All CTR data were updated in the early months of 1999. We completed the task of cleaning these data and supplementing outcome information when necessary. Specifically, the CTR does not list information on recurrence or time to recurrence. We developed a system for identifying cases that received therapy more than one year since the original diagnosis as a screen for recurrent cases.

Task 7: Months 9-12: Select from all available paraffin blocks on each patient, the best specimen (tumor block) for further testing. This will require a review of tumor slides (and preliminary staining) by the pathologist. **COMPLETED**

Task 8: Months 13-24: Laboratory testing on approximately 300 tissue samples. Tests to be done are the following: Histopathologic grade, tumor grade, estrogen receptors, progesterone receptors, DNA ploidy, S phase fraction, presence of p53 mutations, and overexpression of erbB-2. Additionally, gene sequencing will be done on all tumors that are positive for p53 in order to determine location and type of mutation. **COMPLETED**

**UPDATE:**

The testing of Phospho-neu that was reported last year has not yielded meaningful results. Dr. Michael DiGiovanna, another DOD recipient from Yale, completed these tests and covered the costs using other resources. Because the initial findings were not promising, it is unlikely that further work will be done to finalize results of this assay.

Task 9: Months 13-30: Review all original documentation (e.g., progress notes, M.D. consults, discharge summaries), patient interviews for available data on treatment for cancer. Compare these data with CTR data. Fill in the blanks: i.e., contact physicians, specialists, or patients in order to gain as complete information as is possible. **COMPLETED**

Task 10: Months 13-30: This task will be coordinated with task 8, in that a similar review of all available data will be conducted to ascertain vital status (including recurrence or development of subsequent primary cancer). **COMPLETED**

**UPDATE, TASKS 9 AND 10:** These tasks were repeated this year. Once the data analyses were underway, we had questions about the quality of the original data abstraction. The data now available for analysis has been validated using multiple sources of data.

Task 11: Months 12-18: Data Management. Even though the data will be "trickling" in over the next year and one-half, the development of SAS datasets will be underway well in advance of having completed data collection. This will involve the assimilation of several different data sources with existing data to develop SAS data sets, as well as creation of variables, and various indices (especially relevant to the psychosocial variables). **COMPLETED**

**UPDATE:** A PhD-level student biostatistician (Fenghai Duan) joined the study this year (Dr. Ta left the study). He decided to validate much of Dr. Ta's initial data management work. We found some errors in the existing data base. Because the errors were not systematic, we decided that we would repeat much of this work before proceeding with the data analysis. The data management tasks are now complete.



Task 12: Months 18-end of project period: Data Analysis. The timing of this task will depend on the availability of the data. Because of the scope of the proposed project, and the availability of existing data, it is reasonable to plan for data analyses even before all data are available.

**UPDATE:**

The primary data analysis has been completed, yet we continue to identify new uses of these data that will require additional analyses. Preliminary results were presented at both Era of Hope meetings (Washington, Atlanta). See: UPDATED FINDINGS. Because this is a very rich data source, we anticipate publishing many more findings than those presented to date (see planned publications).

Task 13: Year 04: Write-up of results. Clearly, the reporting of results needs to be done in conjunction with on-going analyses. Other than preliminary reports, we anticipate that the major write up will take place in the last year of the study.

**UPDATE:**

One paper submitted; two others will be submitted for publication by 12/31/01. Several others in preparation or planned.

## **KEY RESEARCH ACCOMPLISHMENTS**

### ***Preliminary Findings: NOT for PUBLICATION***

- *Established race difference in survival from breast cancer, after adjustment for stage at diagnosis*
- Established race differences for a number of recognized prognostic indicators: African American women compared to white women are (significantly = \*) more likely to have:
  - \*Later stage at diagnosis
  - \*Larger tumors
  - \*Positive lymph nodes
  - \*Higher histologic grade
  - \*Higher Nuclear grade
  - \*Estrogen Receptor Negative tumors
  - Progesterone Receptor Negative tumors
- Established race differences for a number of genetic alterations that are associated with worse prognosis: African American women compared to white women are (significantly = \*) more likely to have:
  - \*P53 positive tumors
  - C-met positive tumors

Note: African American women were not more likely to be diagnosed with HER-2(neu) positive tumors.

- Specific genetic mutations for P53 seem to differ across race/ethnic groups
- Established race differences for a number of known tumor characteristics that are thought to be associated with poorer prognosis, or at least later stage at diagnosis. Although African American women compared to white women were more likely to have each of the following, these are not statistically significant race differences.
- Survival differences across race groups persist even with adjustment for socioeconomic status (measured as Education)
- In a multivariate model adjusting for established prognostic factors, sociodemographic and treatment variables, the small group of nonreligious subjects was at increased risk for death and traditional faith-healing groups showed a possible protective effect.

### *Update of Preliminary Findings*

This is a population based follow-up study of 145 African American (AA) and 177 white (W) women who were diagnosed with breast cancer between January, 1987 and May, 1989. As of January, 1999, 135 (41.9%) of the women had died with an average time to death of 4.7 years. Eighty-seven (64.4%) of the deaths were confirmed breast cancer deaths. Among survivors, women were followed for a maximum of 11.6 years and an average of 9.2 years. Survival among AA women (56.9%) was significantly lower than survival in W women (68.9%) [age-adjusted Risk Ratio {RR} 1.73 (95% Confidence Interval {CI} 1.21 – 2.48)]. The significant survival disadvantage persisted even with additional adjustment for TNM stage at diagnosis and one measure of socioeconomic status (education) (RR 1.49, 95% CI 1.02 – 2.19).

Several tumor characteristics differed by race group, with African American women more likely to be in the higher risk category. As we have previously reported, African American women were twice as likely to be diagnosed with tumors that were TNM stage II or higher (age-adjusted Odds Ratio [OR] = 2.01, 95% Confidence Interval [CI] 1.24 – 3.24). Evaluating archived tissue specimens, we have demonstrated race differences in a number of other tumor characteristics and genetic alterations: AA women were more likely than W women to have tumors that were higher histologic grade (age-adjusted OR 2.20, 95% CI 1.08 – 4.49), higher nuclear grade (age-adjusted OR = 2.00, 95% CI 1.04 – 3.85), estrogen receptor negative OR = 1.82, 95% CI 1.09 – 3.03, and p53 positive (OR = 4.00, 95% CI 1.77 – 9.01), all of which are generally associated with relatively poor prognosis. Although AA women were more likely than W women to be progesterone receptor negative (61% vs. 50%), and to express c-met (62% vs. 56%), these differences were not statistically significant. AA women were not significantly more likely to be HER-2 [neu] positive. African American women were more likely (not significant) to be positive for a number of known prognostic indicators: necrosis, lymphatic invasion, skin or nipple involvement. Results suggest that after adjustment for TNM stage, only p53 (+) and skin involvement were predictive of survival in African American women, and histologic grade was predictive in White women. Neither c-met or HER-2 (neu) were significantly

associated with survival in this population of women.

*Summary: African American women were significantly more likely to die during the 10- year (approximate) follow-up period than were White women who had been diagnosed with breast cancer in Connecticut in the late 1980s. Tumors in African American women were more likely to be to have characteristics associated with poor prognosis than were white women. The race difference in TNM stage at diagnosis was the strongest explanatory factor for the observed race difference in survival. Race difference in socioeconomic status was not an important explanatory variable. After adjustment for TNM stage at diagnosis, the factors that predict survival may be race specific.*

- Established race difference in survival from breast cancer, after adjustment for stage at diagnosis
- Established race differences for a number of prognostic indicators, confirming earlier reports of a disadvantage for African American women compared to white women
- Earlier results suggest that survival differences persist even with adjustment for socioeconomic status (measured as Education)
- In a multivariate model adjusting for established prognostic factors, sociodemographic and treatment variables, the small group of nonreligious subjects was at increased risk for death and traditional faith-healing groups showed a possible protective effect

Several manuscripts that detail final results are in preparation. One manuscript is under review. Two manuscripts that detail major findings are close to completion and will be submitted to peer reviewed journals by December 31, 2001. Preliminary results have been presented at scientific meetings and as invited presentation (see Appendices). Several other manuscripts are planned.

***Related Invited Presentations (in addition to presented Abstracts included in Appendices)***

*Breast Cancer in African American Women: Race/Ethnic Disparities in Health Outcomes*, State of Connecticut Department of Public Health, Breast and Cervical Cancer Early Detection Program, Health Professions Guest Lecture Series, October 20, 2000

*Race Differences in Breast Cancer Tumor Characteristics*, Sponsored by the American Cancer Society and Yale School of Nursing, December, 2000

***Manuscripts***

Van Ness P, Kasl SV, Jones BA. Religion, Race and Breast Cancer Survival. Under Review.

Jones, BA, Kasl SV, Howe CL, Lachman M. Duan F. Race Differences in Tumor Related Prognostic Factors for Breast Cancer. To be submitted by 12/31/01.

Jones, BA, Kasl SV, Howe CL, Lachman M, Zelterman, D., Duan F. Explaining Race (African American / White) Differences in Survival: The role of selected tumor characteristics and genetic alterations. To be submitted by 12/31/01.

***In Preparation / Planned publications***

Duan F., Zhang H., Jones BA. Analysis of Survival from Breast Cancer using a Tree-based approach.

Jones BA, Beeghly A, Kasl SV, Howe CL, Lachman M. Race / ethnic specific predictors of P53 mutations in breast cancer tumors.

Jones BA, Swede H, Beeghly A, Kasl SV, Howe CL, Lachman M. Race / ethnic specific predictors of HER-2 (neu) overexpression in breast cancer tumors.

Jones BA, Dallal, C, Kasl SV, Howe CL, Lachman M. The role of obesity in explaining lower survival from breast cancer in African American women compared with White women

Jones BA, Kasl SV, Howe CL, Lachman M. Race / ethnic specific predictors of c-met positive breast cancer tumors.

Jones BA, Kasl SV, Howe CL, Lachman M, Duan F. Race / ethnic differences in number of lymph nodes examined: implications for breast cancer survival.

Jones BA, Kasl SV, Duan F. The role of comorbid health conditions in explaining lower survival from breast cancer in African American women compared with White women

Jones BA, Kasl SV, Duan F. The role of treatment course in explaining lower survival from breast cancer in African American women compared with White women

Soler H, Kasl, SV, VanNess P, Jones BA,. The role of psychological factors in explaining lower survival from breast cancer in African American women compared with White women

**Additional manuscripts are anticipated as more detailed analyses are undertaken.**

***Funded Grant Application that Resulted from this work:***

The Patrick and Catherine Weldon Donaghue Medical Research Foundation: *GST Polymorphisms, Race, and Survival from Cancer*, Beth Jones, Principal Investigator, 1/1/02 - 12/31/03, \$180,000

***Research training supported by this work***

These data are currently being used by a predoctoral biostatistics student (Fenghai Duan), and 2 MPH students for theses (C. Dallal, A. Beeghly), and will be used by a postdoctoral fellow (H. Soler) (See Publications/ In preparation or planned.). It is expected that other students will also use these data.

## **REPORTABLE OUTCOMES:**

**Beth A. Jones, Ph.D., Meredith S. Glazer, Ph.D., Stanislav V. Kasl, Ph.D.**

**Yale University School of Medicine**

**RACE DIFFERENCES (BLACK/WHITE)**

**IN BREAST CANCER SURVIVAL. EARLY FINDINGS.**

Abstract presented at the 1997 Era of Hope meeting in Washington, DC.

**Race Differences in Tumor Related Prognostic Factors for Breast Cancer.**

**B.A. Jones\*, S.V. Kasl, C.Howe, M. Lachman , Yale University School of Medicine**

**New Haven, Connecticut 06520.**

**Presenter: BA Jones, TEL: 203-7856-2890, FAX: 203-785-6980**

**Category: Female Cancer**

Abstracts presented at the 1999 Era of Hope Meeting, Atlanta, Georgia (Preliminary Findings)

**Race Differences in Tumor Related Prognostic Factors for Breast Cancer.**

**B.A. Jones\*, S.V. Kasl, C.Howe, M. Lachman , Yale University School of Medicine**

**New Haven, Connecticut 06520.**

**Presenter: BA Jones, TEL: 203-7856-2890, FAX: 203-785-6980**

**Category: Female Cancer**

Presented at the Annual Meeting of the Society of Epidemiologic Research, Baltimore, MD, June, 2000.

## **CONCLUSIONS**

Preliminary results indicate a survival disadvantage for African American women compared with white women with breast cancer, before and after adjustment for stage at diagnosis. Early findings indicate that the survival disadvantage is not explained by race differences in socioeconomic status as measured by years of education. In-depth analyses have been undertaken (some still underway) to determine the prognostic significance of a wide range of factors including medical care, comorbidity, treatment modalities, psychosocial factors, tumor characteristics, and molecular alterations. Outcomes include overall survival and disease free survival over a 10 year (average) follow-up period. This study offers a multidisciplinary approach to understanding the African American /white survival difference in breast cancer.

## **REFERENCE**

Greenlee RT, Hill-Harmon MB, Murray T, Thun M. Cancer statistics, 2001. *Ca: a Cancer Journal for Clinicians* 2001;51(1):15-36.

**APPENDIX A:** Abstracts presented at the 1997 Era of Hope meeting in Washington, D.C.

**RACE DIFFERENCES (BLACK/WHITE)  
IN BREAST CANCER SURVIVAL. EARLY FINDINGS.**

**Beth A. Jones, Ph.D.,  
Meredith S. Glazer, Ph.D., Stanislav V. Kasl, Ph.D.**

**Yale University School of Medicine  
New Haven, Connecticut, 06510-2409**

Despite a somewhat lower incidence of breast cancer in African American women relative to white women, there is a substantial black/white difference in survival from breast cancer. Data from the Surveillance, Epidemiology, and End Results (SEER) program for the years 1986-1992 indicate a five-year survival rate of 85% for white women compared with 70% for black women. While the survival rates for women of both races have improved significantly since the mid 1970s, the survival rates reported for black women in this latest time period are comparable to the survival rates achieved for white women nearly twenty years ago.<sup>1</sup> The purpose of the current investigation is to evaluate the survival in a cohort of black and white women who were diagnosed with breast cancer in Connecticut between 1987 and 1989, and to identify important prognostic factors, with special emphasis on explaining the black/white survival differential.

This follow-up study builds on the results of a completed, population-based investigation aimed at understanding social, psychological, and medical care factors that might explain the observed black/white difference in stage at diagnosis of breast cancer. Previously collected data (from the time of diagnosis) will be combined with newly collected data on molecular alterations (p53 and erbB-2) and tumor characteristics (e.g., DNA ploidy, estrogen receptor status) derived from laboratory testing of archived tissue blocks, as well as vital status information retrieved from the Connecticut Tumor Registry (CTR) to determine the following: 1) predictors of survival from breast cancer for all study subjects; 2) race-specific predictors of survival; and 3) the explanatory potential of prognostic variables in the black/white survival differential.

**Keywords:** Race, Survival, Blacks, Prognostic Factors, Breast Cancer

This work was supported by the U.S. Army Medical Research and Materiel Command under DAMD-17-96-1-6101

## Lay Abstract

This is a population based study of 145 black women and 177 white women who were diagnosed with breast cancer in Connecticut between January, 1987 and May, 1989. Women were identified through active surveillance of 22 Connecticut hospitals. Extensive baseline information was collected from in-person interview and medical chart abstraction. In this first year of the follow-up study, information on vital status and cause of death has been obtained from the CTR. Preliminary data analysis includes bivariate analyses of race and potential prognostic factors using chi-square tests; predictors of survival have been evaluated with Kaplan-Meier product limit estimates and Cox proportional hazards models. In these preliminary analyses, all cause mortality is the outcome variable.

As of January, 1997, 113 women of the 322 breast cancer cases (35.1%) had died, with an average time to death of 4.2 years. Eighty-two (72%) of the deaths were confirmed breast cancer deaths. Among survivors, women were followed for a maximum of 9.6 years with an average follow-up of 7.2 years. Black women were significantly more likely to die than were white women during the follow-up period (age-adjusted Risk Ratio [RR] = 1.70, Confidence Interval [CI], 1.16-2.50). Although adjustment for stage at diagnosis (*in situ*/ local vs. regional/remote) reduced the predictive value of race, black women were still significantly more likely to die from their disease than were their white counterparts (RR = 1.52, CI 1.03-2.24). Further adjustment of this model for one measure of socioeconomic status (years of education) did not alter these results.

Several tumor characteristics differed by race group, with black women more likely to be in the higher risk category. Using data abstracted from the medical chart, and adjusting for age, black women were more likely to have high grade tumors (Odds Ratio [OR] = 2.53, CI 1.08-5.91), lymphatic invasion (OR = 1.91, CI 0.99-3.69), necrosis (OR=1.48, CI 0.87-2.53), skin involvement 1.88 (0.66-5.36), nipple involvement (OR = 1.95, CI 0.77-4.99), estrogen receptor (ER) negative tumors (OR = 1.29, CI 0.70-2.39), and progesterone receptor (PR) negative tumors (OR= 1.50, CI 0.81-2.78). While several of these factors do not differ significantly between race groups, they suggest a tendency toward more aggressive tumors in black women. The lack of statistical significance may be a function of missing data as not all laboratory tests were performed on all tumors. Of the tumor characteristics listed above, only skin involvement remained a significant predictor of mortality after adjustment for age, race, and stage at diagnosis.

These preliminary results demonstrate a survival disadvantage for black women compared with white women with breast cancer, before and after adjustment for stage at diagnosis. Early findings suggest that the survival differential is not explained by race differences in socioeconomic status as measured with years of education. Over the course of the study, these findings will be expanded using more complete data on vital status, cause of death, and time to recurrence. Additionally, we will evaluate the prognostic significance of a wide range of factors including medical care and psychosocial variables, other tumor characteristics, and molecular alterations, thus permitting a multidisciplinary approach to understanding the black/white survival difference in breast cancer.

**Appendix B: Abstracts presented at the 1999 Era of Hope Meeting, Atlanta, Georgia**  
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## Race Differences in Tumor Related Prognostic Factors for Breast Cancer

Beth A. Jones, Stanislav V. Kasl, Christine Howe, Mary Lachman, Fenghai Duan  
 Yale University School of Medicine  
 New Haven, Connecticut  
 Email: [Beth.Jones@Yale.edu](mailto:Beth.Jones@Yale.edu), Telephone: 203-785-2890

This is a population based follow-up study of 145 African American (AA) and 177 white (W) women who were diagnosed with breast cancer between January, 1987 and May, 1989. As of January, 1999, 135 (41.9%) of the women had died with an average time to death of 4.7 years. Eighty-seven (64.4%) of the deaths were confirmed breast cancer deaths. Among survivors, women were followed for a maximum of 11.6 years and an average of 9.2 years. Survival among AA women (56.9%) was significantly lower than survival in W women (68.9%) [age-adjusted Risk Ratio {RR} 1.73 (95% Confidence Interval {CI} 1.21 – 2.48)]. The significant survival disadvantage persisted even with additional adjustment for TNM stage at diagnosis and one measure of socioeconomic status (education) (RR 1.49, 95% CI 1.02 – 2.19).

Several tumor characteristics differed by race group, with African American women more likely to be in the higher risk category. As we have previously reported, African American women were twice as likely to be diagnosed with tumors that were TNM stage II or higher (age-adjusted Odds Ratio [OR] = 2.01, 95% Confidence Interval [CI] 1.24 – 3.24). Evaluating archived tissue specimens, we have demonstrated race differences in a number of other tumor characteristics and genetic alterations: AA women were more likely than W women to have tumors that were higher histologic grade (age-adjusted OR 2.20, 95% CI 1.08 – 4.49), higher nuclear grade (age-adjusted OR = 2.00, 95% CI 1.04 – 3.85), estrogen receptor negative OR = 1.82, 95% CI 1.09 – 3.03, and p53 positive (OR = 4.00, 95% CI 1.77 – 9.01), all of which are generally associated with relatively poor prognosis. Although AA women were more likely than W women to be progesterone receptor negative (61% vs. 50%), and to express c-met (62% vs. 56%), these differences were not statistically significant. AA women were not significantly more likely to be HER-2 [neu] positive. African American women were more likely (not significant) to be positive for a number of known prognostic indicators: necrosis, lymphatic invasion, skin or nipple involvement. Results suggest that after adjustment for TNM stage, only p53 (+) and skin involvement were predictive of survival in African American women, and histologic grade was predictive in White women. Neither c-met or HER-2 (neu) were significantly associated with survival in this population of women.

**Summary:** African American women were significantly more likely to die during the 10- year (approximate) follow-up period than were White women who had been diagnosed with breast cancer in Connecticut in the late 1980s. Tumors in African American women were more likely to be to have characteristics associated with poor prognosis than were white women. The race difference in TNM stage at diagnosis was the strongest explanatory factor for the observed race difference in survival. Race difference in socioeconomic status was not an important explanatory variable. After adjustment for TNM stage at diagnosis, the factors that predict survival may be race specific.

DAMD17-96-1-6101

**Appendix C: Abstract presented at the Society for Epidemiology Annual Meeting, Baltimore, MD, June, 2000.**

**Race Differences in Tumor Related Prognostic Factors for Breast Cancer.**

**B.A. Jones\*, S.V. Kasl, C.Howe, M. Lachman , Yale University School of Medicine  
New Haven, Connecticut 06520.**

**Presenter: BA Jones, TEL: 203-7856-2890, FAX: 203-785-6980**

**Category: Female Cancer**

This is a population based survival study of 145 African American (AA) and 177 white (W) women diagnosed with breast cancer in Connecticut between 1987 and 1989. As of January, 1999, 132 (41.0%) of women had died with an average time to death of 4.7 years. Survival among AA women (51.7%) was significantly lower than survival in W women (65.0%) [age-adjusted Risk Ratio {RR} 1.82,  $p = .001$ ]. The significant survival disadvantage persisted even with adjustment for age, TNM stage at diagnosis and one measure of socioeconomic status (education) [RR = 1.62,  $p = .01$ ]. AA women were twice as likely to be diagnosed with tumors that were TNM stage II or higher (Odds Ratio [OR] = 2.06, 95% Confidence Interval [CI] 1.29 – 3.30). Evaluating archived tissue specimens, we demonstrated race differences in a number of tumor characteristics and genetic alterations: AA women were more likely than W women to have tumors that were higher histologic grade ( $p = .027$ ), higher nuclear grade ( $p = .054$ ), estrogen receptor negative ( $p = .019$ ), and p53 positive ( $p = .001$ ), all of which are generally associated with relatively poor prognosis. Although AA women were more likely than W women to be progesterone receptor negative (70% vs. 63%), and to express c-met (62% vs. 55%), differences were not statistically significant. AA women were not significantly more likely to be neu positive. Results suggest that p53 (+), progesterone receptor status (-), histologic grade (2 or 3), and nuclear grade (2 or 3) were predictive of poorer survival, particularly among AA women. C-met and neu were not significantly associated with survival in this population.

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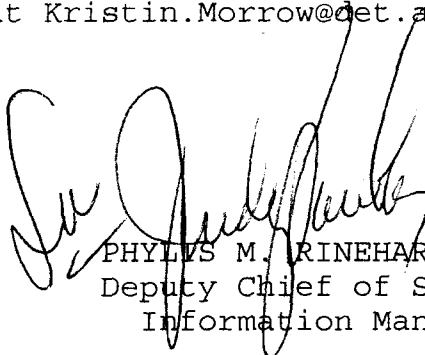
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